HEPATIC GSH IN HEXACHLOROBENZENE-INDUCED PORPHYRIA.[1]

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In the biosynthesis of heme, irreversible oxidation of the intermediate porphyrinogens is believed to be prevented by cellular antioxidant systems such as GSH (Heikel et al., 1958; Mauzerall and Granick, 1958). Administration of halogenated benzene compounds, which are conjugated and excreted as mercaptide derivatives (Williams, 1959), was shown to result in transient reduction of GSH in the liver (Binet and Wellers, 1951; Barnes and James, 1957). Since chronic poisoning with hexachlorobenzene (HCB) leads to hepatic formation and urinary excretion of large amounts of porphyrins (Ockner and Schmid, 1961) it was tempting to speculate that this disturbance of pigment metabolism might be due to a deficiency in hepatic GSH.

Adult male Sprague-Dawley rats were fed ad lib. ground "Purina Rat Chow" containing 0.2% HCB. Total urinary porphyrins were determined spectrophotometrically (Rimington and Sveinsson, 1950) on a 24-hour urine sample collected 2 days before sacrifice. The animals were killed by a blow to the head and the liver was quickly removed and cooled. One gram of liver was homogenized in ice-cold 3% sulphosalicylic acid, centrifuged and the supernatant assayed in duplicate for GSH (Martin and McIlwain, 1959). With each assay, controls were performed with freshly prepared standard solutions of GSH (Sigma). Recovery experiments yielded 98 to 102% of the GSH added to liver homogenates, and in all instances assays on duplicate samples prepared from the same rat agreed within 5%.

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The results given in Table 1 reveal that in rats with HCB-induced porphyrinuria, hepatic GSH concentration was not reduced and total GSH in the liver was increased. This indicates that under these experimental conditions, increased formation of porphyrins in the liver is not the result of GSH deficiency.

Table 1

Hepatic GSH and urinary porphyrins in male rats fed HCB.

Initial weight gm	Days fed HCB	Weight on sacrifice gm	Liver weight gm	GSH mg/100 gm wet liver	Total liver GSH, mg	Urine* porphyrins µg/24 hours
520	0	520	15.0	233	35	< 15
308	0	308	11.0	264	29	< 15
230	26	297	21.5	283	61	< 15
228	26	288	20.0	235	47	< 15
234	37	305	25.1	290	73	39.5
208	37	247	25.2	385	97	24.6
222	54	232	21.2	387	82	154
224	54	265	20.7	285	59	205

* Including all preformed ether-soluble and insoluble porphyrins.

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